cancer, gastric cancer, colorectal cancer, throat cancer, cancer of the urinary tract, cancer of the reproductive tract, esophageal cancer, and bronchiogenic carcinoma.

REMARKS

Justification for the amendments is as follows. The claims were amended to correct typographical errors. No new matter is added by any of these amendments. Attached hereto is a marked-up version of the changes made by the present amendment. The attached page is captioned "Version with markings to show changes made."

I. Restriction Requirement

Claims 1-36 were originally filed and are subject to a Restriction Requirement. Claims 1-36 are pending. In the Restriction Requirement, the Examiner restricted the claims as follows:

Group I: Claims 1-3 and 36 in part, drawn to methods of treating glioma using an agent that affects laminin 5 processing by BMP-1;

Group II: Claims 1, 2, 4-10, 14, 36 in part, drawn to methods of treating squamous cell carcinoma using an agent that affects laminin 5 processing by BMP-1;

Group III: Claims 1, 2, 4-9, 11-14, 36 in part, drawn to methods of treating squamous cell carcinoma using an agent that affects laminin 5 processing by a BMP-1 related protein or mTld;

Group IV: Claims 15-17, drawn to compositions comprising an agent that affects laminin 5 processing by a BMP-1 related protein;

Group V: Claims 18-24, drawn to methods of diagnosing a condition by detecting expression of a BMP-1 related protein;

Group VI: Claim 25, drawn to diagnostic kits;

Group VII: Claims 26 and 31, drawn to methods of screening for an agent that affects laminin 5 processing by BMP-1 related proteins;

Group VIII: Claims 27, 32-35, drawn to isolated polypeptides comprising BMP-1 cleavage sequence;

Group IX: Claims 28 and 29, drawn to isolated polynucleotides; and

Group X: Claim 30, drawn to antibodies.

In view of the following remarks, Applicants respectfully request that the Examiner reconsider and withdraw the requirement for restriction at least among Groups I, II, and III. Specifically, a requirement for restriction is proper if the inventions are independent and distinct as claimed, and if examination of the inventions together would result in a serious burden to the Examiner if restriction were not required.

Applicants respectfully submit that, as no serious burden to the Examiner would result from examination of the inventions of Groups I, II, and III, these requirements for proper restriction have not been met.

The M.P.E.P. states that, "[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine [the application] on the merits, even though it includes claims to independent or distinct inventions." (M.P.E.P. 803, p. 800-3, 7th Edition, February 2000.) Applicants respectfully submit that, in view of the interrelatedness of the subject matter pertaining to agents that affect processing of laminin 5 by BMP-1 related enzymes, methods of identifying the agents in screening assays, and methods of using the agents in therapeutic methods, it would be no serious burden to the Examiner to search and examine claims 1-14 and 36, the claims of Groups I, II, and III, together and in their entirety.

Groups I-III, encompassing claims 1-14 and 36, recite methods of treating disorders by administering an agent that effects processing of laminin 5 by a BMP-1 related protein. As clearly established in the present application, the BMP-1 related enzymes, including BMP-1, mTld, mTll-1, and mTll-2, share significant structural and functional homology. In point of fact, BMP-1 and mTld are splice variants encoded by the same gene. (See, e.g., the specification at page 5, lines 20 to 21; and Finelli et al. (1995) Genetics 141:271-281.) The BMP-1 related enzymes also have similar activities, as described throughout the specification with respect to processing of laminin 5 $\alpha 3$ and $\gamma 2$ subunits. Additionally, small molecule agents and antibodies show cross-reactivity with the different members of the BMP-1 related enzymes, as exemplified generally throughout the specification, e.g., in the inhibitory activity of compounds 1, 2, and 3, and in the binding activity of antibody. (See, e.g., page 27, line 17 to 27; page 64, lines 9 to 11, etc.) Therefore, due to the interrelatedness of the enzymes and their laminin 5 processing activity, it would not be a serious burden to examine the claims of Groups I-III together.

In summary, in view of the preceding remarks, Applicants request reconsideration and withdrawal of the restriction requirement, at least as it applies to the claims 1-14 and 36, the claims of Groups I, II, and III. However, in order to comply with the provisions of 37 C.F.R. 1.143, Applicants hereby provisionally elect, with traverse, to pursue the subject matter corresponding to the claims of Group III, claims 1, 2, 4-9, 11-14, and 36 in part. Applicants reserve without prejudice the right to pursue any non-elected subject matter in continuing applications.

II. Species Election

The Examiner stated that claim 5 is "generic to a plurality of disclosed patentably distinct species comprising epithelial cells" and required election of a single disclosed species. (Restriction Requirment, page 5.) Similarly, the Examiner stated that claim 7 is "generic to a plurality of disclosed patentably distinct species comprising squamous cell carcinoma" and required election to a single disclosed species. (Restriction Requirement, page 6.)

It is Applicants' understanding that the species election is a provisional election, and that the provisional election will only be given effect in the event that the generic claim is found not allowable. (See 37 C.F.R. 1.146.) As stated by the Examiner, claim 5 is generic to "epithelial cells" and claim 7 is generic to "squamous cell carcinoma." Therefore, Applicants hereby provisionally elect, with traverse, the species corresponding to mucosal epithelial cells (claim 5) and oral squamous cell carcinoma (claim 7). Upon allowance of the generic claims, Applicants request consideration of claims to additional species that include all the limitations of the allowed generic claims as provided by 37 C.F.R. 1.141.

Applicants reserve without prejudice the right to pursue any non-elected subject matter in continuing applications.

CONCLUSION

If there are any questions regarding the present communication or the above-referenced application, please call Applicants' Agent at 650-866-7265.

Applicants believe that no fee is due with this communication. If, however, the Commissioner determines that a fee is due, the Commissioner is hereby authorized to charge any necessary fees to Deposit Account No. **50-0811**. **This form is enclosed in duplicate.**

Respectfully submitted,
FibroGen, Inc.

DATE: 20 February 03

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Claims 4 and 7 have been replaced with the following rewritten claims:

4. A method of treating a condition characterized by [a] neoplastic epithelial cells, the method comprising administering to a subject in need an effective amount of an agent that affects processing of laminin 5 by a BMP-1 related protein.

7. The method of claim 6, wherein the squamous cell carcinoma is selected from the group consisting of skin cancer, lung cancer, head cancer, neck cancer, oral cancer, cervical cancer, tongue cancer, gastric cancer, colorectal cancer, throat cancer, cancer of the urinary tract, cancer of the reproductive tract, esophageal cancer, [throat cancer,] and bronchiogenic carcinoma.